

SEQUENCE LISTING

<110> Maxygen ApS
 Maxygen Holdings Ltd.
 Haaning, Jesper Mortensen
 Andersen, Kim Vilbour
 Röpke, Mads
 Glazer, Steven

<120> FVII or FVIIa Variants

<130> 0272wo310

<150> US 60/456,547
 <151> 2003-03-20

<150> US 60/479,708
 <151> 2003-06-19

<160> 19

<170> PatentIn version 3.2

<210> 1

<211> 1338

<212> DNA

<213> Homo sapiens

<220>

<221> CDS

<222> (115)..(1338)

<400> 1			
atggtcagcc aggccctccg cctcctgtgc ctgctcctgg ggctgcaggg ctgcctggct		60	
gccgtttcg tcacccagga ggaagcccat ggcttcctgc atcgccggcg ccgg gcc		117	
Ala			
1			
aat gcc ttt ctg gaa gag ctc cgc cct ggc tcc ctg gaa cgc gaa tgc		165	
Asn Ala Phe Leu Glu Glu Leu Arg Pro Gly Ser Leu Glu Arg Glu Cys			
5	10	15	
aaa gag gaa cag tgc agc ttt gag gaa gcc cgg gag att ttc aaa gac		213	
Lys Glu Glu Gln Cys Ser Phe Glu Glu Ala Arg Glu Ile Phe Lys Asp			
20	25	30	
gct gag cgg acc aaa ctg ttt tgg att agc tat agc gat ggc gat cag		261	
Ala Glu Arg Thr Lys Leu Phe Trp Ile Ser Tyr Ser Asp Gly Asp Gln			
35	40	45	
tgc gcc tcc agc cct tgc cag aac ggg ggc tcc tgc aaa gac cag ctg		309	
Cys Ala Ser Ser Pro Cys Gln Asn Gly Gly Ser Cys Lys Asp Gln Leu			
50	55	60	65
cag agc tat atc tgc ttc tgc ctg cct gcc ttt gag ggg cgc aat tgc		357	
Gln Ser Tyr Ile Cys Phe Cys Leu Pro Ala Phe Glu Gly Arg Asn Cys			
70	75	80	
gaa acc cat aag gat gac cag ctg att tgc gtc aac gaa aac ggg ggc		405	
Glu Thr His Lys Asp Asp Gln Leu Ile Cys Val Asn Glu Asn Gly Gly			
85	90	95	
tgc gag cag tac tgc agc gat cac acg ggc acg aag cgg agc tgc cgc		453	
Cys Glu Gln Tyr Cys Ser Asp His Thr Gly Thr Lys Arg Ser Cys Arg			
100	105	110	
tgc cac gaa ggc tat agc ctc ctg gct gac ggg gtg tcc tgc acg ccc		501	

Cys His Glu Gly Tyr Ser Leu Leu Ala Asp Gly Val Ser Cys Thr Pro			
115	120	125	
acg gtg gaa tac cct tgc ggg aag att ccc att cta gaa aag cggtt aac			549
Thr Val Glu Tyr Pro Cys Gly Lys Ile Pro Ile Leu Glu Lys Arg Asn			
130	135	140	145
gct agc aaa ccc cag ggc cggtt atc gtc ggc ggg aag gtc tgc cct aag			597
Ala Ser Lys Pro Gln Gly Arg Ile Val Gly Gly Lys Val Cys Pro Lys			
150	155	160	
ggg gag tgc ccc tgg cag gtc ctg ctc ctg gtc aac ggg gcc cag ctg			645
Gly Glu Cys Pro Trp Gln Val Leu Leu Val Asn Gly Ala Gln Leu			
165	170	175	
tgc ggc ggg acc ctc atc aat acc att tgg gtc gtg tcc gcc gct cac			693
Cys Gly Gly Thr Leu Ile Asn Thr Ile Trp Val Val Ser Ala Ala His			
180	185	190	
tgc ttc gat aag att aag aat tgg cggtt aac ctc atc gct gtg ctc ggc			741
Cys Phe Asp Lys Ile Lys Asn Trp Arg Asn Leu Ile Ala Val Leu Gly			
195	200	205	
gaa cac gat ctg tcc gag cat gac ggg gac gaa cag tcc cgc cggtt			789
Glu His Asp Leu Ser Glu His Asp Gly Asp Glu Gln Ser Arg Arg Val			
210	215	220	225
gct cag gtc atc att ccc tcc acc tat gtg cct ggc acg acc aat cac			837
Ala Gln Val Ile Ile Pro Ser Thr Tyr Val Pro Gly Thr Thr Asn His			
230	235	240	
gat atc gct ctg ctc cgc ctc cac cag ccc gtc gtg ctc acc gat cac			885
Asp Ile Ala Leu Leu Arg Leu His Gln Pro Val Val Leu Thr Asp His			
245	250	255	
gtc gtg cct ctg tgc ctc gag cggtt acc ttt agc gaa cgc acg ctg			933
Val Val Pro Leu Cys Leu Pro Glu Arg Thr Phe Ser Glu Arg Thr Leu			
260	265	270	
gct ttc gtc cgc ttt agc ctc gtg tcc ggc tgg ggc cag ctg ctc gac			981
Ala Phe Val Arg Phe Ser Leu Val Ser Gly Trp Gly Gln Leu Leu Asp			
275	280	285	
cgg ggc gct acc gct ctc gag ctg atg gtg ctc aac gtc ccc cggtt			1029
Arg Gly Ala Thr Ala Leu Glu Leu Met Val Leu Asn Val Pro Arg Leu			
290	295	300	305
atg acc cag gac tgc ctg cag cag tcc cgc aaa gtg ggg gac tcc ccc			1077
Met Thr Gln Asp Cys Leu Gln Ser Arg Lys Val Gly Asp Ser Pro			
310	315	320	
aat atc acg gag tat atg ttt tgc gct ggc tat agc gat ggc tcc aag			1125
Asn Ile Thr Glu Tyr Met Phe Cys Ala Gly Tyr Ser Asp Gly Ser Lys			
325	330	335	
gat agc tgc aag ggg gac tcc ggc ggg ccc cat gcc acg cac tat cgc			1173
Asp Ser Cys Lys Gly Asp Ser Gly Gly Pro His Ala Thr His Tyr Arg			
340	345	350	
ggg acc tgg tac ctc acc ggg atc gtc agc tgg ggc cag ggc tgc gcc			1221
Gly Thr Trp Tyr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys Ala			
355	360	365	
acg gtg ggg cac ttt ggc gtc tac acg cgc gtc agc cag tac att gag			1269
Thr Val Gly His Phe Gly Val Tyr Thr Arg Val Ser Gln Tyr Ile Glu			
370	375	380	385
tgg ctg cag aag ctc atg cggtt agc gaa ccc cggtt ccc ggg gtg ctc ctg			1317
Trp Leu Gln Lys Leu Met Arg Ser Glu Pro Arg Pro Gly Val Leu Leu			

390

395

400

cgg gcc cct ttc cct tga taa
Arg Ala Pro Phe Pro
405

1338

<210> 2
<211> 406
<212> PRT
<213> Homo sapiens

<400> 2

Ala Asn Ala Phe Leu Glu Glu Leu Arg Pro Gly Ser Leu Glu Arg Glu
1 5 10 15

Cys Lys Glu Glu Gln Cys Ser Phe Glu Glu Ala Arg Glu Ile Phe Lys
20 25 30

Asp Ala Glu Arg Thr Lys Leu Phe Trp Ile Ser Tyr Ser Asp Gly Asp
35 40 45

Gln Cys Ala Ser Ser Pro Cys Gln Asn Gly Gly Ser Cys Lys Asp Gln
50 55 60

Leu Gln Ser Tyr Ile Cys Phe Cys Leu Pro Ala Phe Glu Gly Arg Asn
65 70 75 80

Cys Glu Thr His Lys Asp Asp Gln Leu Ile Cys Val Asn Glu Asn Gly
85 90 95

Gly Cys Glu Gln Tyr Cys Ser Asp His Thr Gly Thr Lys Arg Ser Cys
100 105 110

Arg Cys His Glu Gly Tyr Ser Leu Leu Ala Asp Gly Val Ser Cys Thr
115 120 125

Pro Thr Val Glu Tyr Pro Cys Gly Lys Ile Pro Ile Leu Glu Lys Arg
130 135 140

Asn Ala Ser Lys Pro Gln Gly Arg Ile Val Gly Gly Lys Val Cys Pro
145 150 155 160

Lys Gly Glu Cys Pro Trp Gln Val Leu Leu Leu Val Asn Gly Ala Gln
165 170 175

Leu Cys Gly Gly Thr Leu Ile Asn Thr Ile Trp Val Val Ser Ala Ala
180 185 190

His Cys Phe Asp Lys Ile Lys Asn Trp Arg Asn Leu Ile Ala Val Leu
195 200 205

Gly Glu His Asp Leu Ser Glu His Asp Gly Asp Glu Gln Ser Arg Arg
210 215 220

Val Ala Gln Val Ile Ile Pro Ser Thr Tyr Val Pro Gly Thr Thr Asn
225 230 235 240

His Asp Ile Ala Leu Leu Arg Leu His Gln Pro Val Val Leu Thr Asp
245 250 255

His Val Val Pro Leu Cys Leu Pro Glu Arg Thr Phe Ser Glu Arg Thr
260 265 270

Leu Ala Phe Val Arg Phe Ser Leu Val Ser Gly Trp Gly Gln Leu Leu
275 280 285

Asp Arg Gly Ala Thr Ala Leu Glu Leu Met Val Leu Asn Val Pro Arg
290 295 300

Leu Met Thr Gln Asp Cys Leu Gln Gln Ser Arg Lys Val Gly Asp Ser
305 310 315 320

Pro Asn Ile Thr Glu Tyr Met Phe Cys Ala Gly Tyr Ser Asp Gly Ser
325 330 335

Lys Asp Ser Cys Lys Gly Asp Ser Gly Gly Pro His Ala Thr His Tyr
340 345 350

Arg Gly Thr Trp Tyr Leu Thr Gly Ile Val Ser Trp Gly Gln Gly Cys
355 360 365

Ala Thr Val Gly His Phe Gly Val Tyr Thr Arg Val Ser Gln Tyr Ile
370 375 380

Glu Trp Leu Gln Lys Leu Met Arg Ser Glu Pro Arg Pro Gly Val Leu
385 390 395 400

Leu Arg Ala Pro Phe Pro
405

<210> 3
<211> 1357

<212> DNA

1330

<223> Synthetic gene for optimized expression of hFVII

<400> 3

ggatccgccc accatggtca gccaggccct ccgcctcctg tgccctgtcc tggggctgca 60

gggctgcctg gctgccgtct tcgtcaccca ggaggaagcc catggcgtcc tgcatcgccg 120

gccccggggcc aatgcctttc tgaaagagct ccgcccctggc tccctggaaac gcgaatgcaa 180

agaggaacag tgcatgtttg aggaagcccg ggagattttc aaagacgctg agcggaccaa 240

actgttttgg attagctata gcgatggcga tcagtgcgcc tccagccctt gccagaacgg . 300

gggctcctgc aaagaccaggc tgccagagcta tatctgtttc tgccctgcctg cctttgaggg 360

gcgcaattgc gaaaccata aggatgacca gctgatttc	gtcaacgaaa acggggctg	420
cgagcagtac tgcagcgatc acacgggcac gaagcggagc	tgccgctgcc acgaaggcta	480
tagcctcctg gctgacgggg tgtcctgcac gcccacggtg	gaataaccctt gcgggaagat	540
tcccattcta gaaaagcggta acgctagcaa accccaggc	cggatcgctg gcgggaaggt	600
ctgcccataag ggggagtgcc cctggcaggt cctgctcctg	gtcaacgggg cccagctgtg	660
cggcgggacc ctcataata ccattgggt cgtgtccgcc	gctcactgct tcgataagat	720
taagaattgg cgaaacctca tcgctgtgct cggcgaacac	gatctgtccg agcatgacgg	780
ggacgaacag tccccccggg tggctcaggt catcattccc	tccacctatg tgccctggcac	840
gaccaatcac gatatcgctc tgctccgcct ccaccagccc	gtcgtgctca ccgatcacgt	900
cgtgcctctg tgccctgcctg agcggacctt tagcgaacgc	acgctggctt tcgtccgcct	960
tagcctcgtg tccggctggg gccagctgct cgaccggggc	gctaccgctc tcgagctgat	1020
ggtgctcaac gtccccccggc tgatgaccca ggactgcctg	cagcagtccc gcaaagtggg	1080
ggactcccccc aatatcacgg agtatatgtt ttgcgctggc	tatagcgatg gctccaagga	1140
tagctgcaag ggggactccg gccccccca tgccacgcac	tatcgccggta cctggctacac	1200
caccgggatc gtcagctggg gccagggctg cgccacggtg	gggcactttg gcgtctacac	1260
gcgcgtcagc cagtacattg agtggctgca gaagctcatg	cggagcgaac cccggcccccgg	1320
ggtgctcctg cgggccccctt tcccttgata aaagctt		1357

<210> 4
<211> 31
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 4
agctggcttag ccactggca ggtaagtatc a 31

<210> 5
<211> 31
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 5
tggcgggatc cttaagagct gtaattgaac t 31

<210> 6
<211> 38
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 6

cccattctag aaaagcgaa cgccagcaaa ccccaggg

38

<210> 7
<211> 34
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 7
ccaattctta atcttgttga agcagtgagc ggcg

34

<210> 8
<211> 21
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 8
ctccgtata ttggggaggc

21

<210> 9
<211> 34
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 9
cgccgctcac tgcttcaaca agattaagaa ttgg

34

<210> 10
<211> 22
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 10
cgctctcgag ctgatggtgc tc

22

<210> 11
<211> 22
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 11
caaacaacag atggctggca ac

22

<210> 12
<211> 34
<212> DNA
<213> Artificial

<220>

<223> Primer

<400> 12
cgccgctcac tgcttcaaga agattaagaa ttgg 34

<210> 13
<211> 34
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 13
ccaattctta atcttcttga agcagtgagc ggcg 34

<210> 14
<211> 33
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 14
ctccacacctat gtgcctctga cgaccaatca cga 33

<210> 15
<211> 33
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 15
tcgtgattgg tcgtcagagg cacataggtg gag 33

<210> 16
<211> 29
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 16
ccaaggatgc cagggggact ccggcgggc 29

<210> 17
<211> 33
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 17
gccccccgga gtccccctgg cagcttatcct tgg 33

<210> 18
<211> 36
<212> DNA

<213> Artificial

<220>
<223> Primer

<400> 18
accttatgtgc ctggcgctgc cacgaccaat cacgat

36

<210> 19
<211> 36
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 19
atcgtgattt gtcgtggcag cgccaggcac ataggt

36